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MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/599,087	LUETHY ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *3-8* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20031120*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed November 20, 2003 is acknowledged and has been entered. Claims 1-3 have been amended.

2. Claims 1-8 are pending in the application

3. Claims 1, 2, and claims 3-8, insofar as the claims are drawn to an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 5, are currently under continued prosecution.

Information Disclosure Statement

4. The information disclosure filed November 20, 2003 has been considered. An initialed copy is enclosed.

Election/Restrictions

5. Newly amended claims 3-8 are directed, in part, to inventions that are independent or distinct from the invention originally claimed for the following reasons:

Claim 3 is drawn to a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5, wherein the amino acid at position 12 may be methionine, rather than isoleucine; the amino acid at position 18 may be cysteine, rather than serine; the amino acid at position 22 may be serine, rather than threonine; the amino acid at position 25, 61, or 64 may be arginine, rather than lysine; the amino acid at position 26 may be lysine, rather than arginine; the amino acid at position 27 may be histidine, rather than arginine; the amino acid at position 51 may be threonine, rather than asparagine; the amino acid at position 55 may be asparagine, rather than histidine; the amino acid at position 81 may be isoleucine, rather than valine; and the amino acids at any one or more of positions 5, 8, 10, 11, 14, 17, 20, 31-34, 36-40, 43, 44, 46-50, 52, 57, 59, 62, and 65-71 may be any

naturally occurring amino acid, rather than the amino acid at those positions in SEQ ID NO: 5. Therefore, while claim 3 encompasses the elected invention, i.e., a nucleic acid molecule comprising a polynucleotide sequence encoding a polypeptide comprising the amino acid sequence set forth as SEQ ID NO: 5, claim 3 also encompasses a multitude of other nucleic acid molecules comprising polynucleotide sequences encoding polypeptides comprising amino acid sequences that differ from the amino acid sequence set forth as SEQ ID NO: 5 at any one or more of the positions to which claim 3 specifically refers. Each of the multitude of nucleic acid molecules encompassed by claim 3, which have an amino acid sequence differing from the amino acid sequence set forth as SEQ ID NO: 5 is distinct from the elected invention, and the search required to examine any of these distinct inventions is different than the search that has been required to search the elected invention. As the need to perform additional searches constitutes serious burden, it is proper to withdraw these distinct inventions from consideration.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, to the extent that claims 3-8 are drawn to any nucleic acid molecule encompassed by claim 3, which encodes a polypeptide having an amino acid sequence that differs from the amino acid sequence set forth as SEQ ID NO: 5, claims 3-8 are withdrawn from consideration as being directed to a non-elected invention. In other words, claim 3 is only considered herein to the extent that the claim is drawn to the elected invention, i.e., a nucleic acid molecule comprising a polynucleotide sequence encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5. See 37 CFR 1.142(b) and MPEP § 821.03.

At pages 15-17, Applicant sets forth arguments that the full scope of the subject matter recited in claim 3 should be considered. Applicant has argued that as original claim 3 encompasses each and every member of the genus of nucleic acid molecules encompassed by claim 3 presently, claim 3 does not encompass a multitude of inventions, which are distinct from the elected invention.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Original claim 3 specifically encompassed a genus of nucleic acid molecules comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 5, but for at least one conservative amino acid substitution. However, presently claim 3 encompasses a nucleic acid molecule comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 5, but for the substitution of the asparagine residue at position 51 by a threonine residue. As is well known in the art and as the specification teaches at page 19, the substitution of asparagine by threonine is not a conservative substitution, because a conservative substitution involves the substitution of one amino acid for another having about the same charge and polarity as the original amino acid. Thus, contrary to Applicant's assertion, original claim 3 did not encompass each and every member of the genus of nucleic acid molecules encompassed by claim 3 presently, as the nucleic acid molecule comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 5, but for the substitution of the asparagine residue at position 51 by a threonine residue, which is presently encompassed by claim 3, was not encompassed by original claim 3. In addition, presently claim 3 also encompasses any nucleic acid molecule comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 5, but for the substitution of the amino acid residue at any of one or more of positions 5, 8, 10, 11, 14, 17, 20, 31-34, 36-40, 43, 44, 46-50, 52, 57, 59, 62, and 65-71 by any *other* naturally occurring amino acid, so the substitution need not be a conservative substitution. The nucleic acid molecules comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 5, but for the substitution of the amino acid residue at any of one or more of positions 5, 8, 10, 11, 14, 17, 20, 31-34, 36-40, 43, 44, 46-50, 52, 57, 59, 62, and 65-71 by another naturally occurring amino acid having different charge and/or polarity, which are presently encompassed by claim 3, were not encompassed by original claim 3. In this regard therefore claim 3 is presently recites a broader scope than original claim 3.

In further reply to Applicant's arguments, the search required to examine original claim 3 and the search required to examine the extent of claim 3 encompassing any nucleic acid molecule, which encodes a polypeptide having an amino acid sequence that differs from the amino acid sequence set forth as SEQ ID NO: 5, are not co-extensive or the same. Searching the elected invention required searching databases using SEQ ID NO: 5 as a query; searching each of the other distinct nucleic acid molecules encompassed by claim 3 would require an additional and different search using the distinct amino acid sequence of the polypeptide encoded by the other nucleic acid molecule. Thus, any subject matter encompassed by claim 3, which is different from the subject matter of the elected invention, has not so far been searched or considered; nor will it be, as Applicant has received an action on the merits for the originally presented invention, which invention has been constructively elected by original presentation for prosecution on the merits in this Office action. See 37 CFR § 1.142(b) and MPEP § 821.03.

Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed May 20, 2003 have been withdrawn.

Specification

7. The specification is objected to because American Type Culture Collection™ is not properly demarcated as a trademark at page 2 in line 1. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Appropriate corrections are required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine

under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

Claim Objections

8. Claims 3-8 are objected to for the following reason: Applicant has received an action on the merits for the originally presented invention, which invention has been constructively elected by original presentation for prosecution on the merits in this Office action. See 37 CFR § 1.142(b) and MPEP § 821.03. Accordingly, claim 3 is drawn to the subject matter of non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 5 and 6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 5 and 6 are drawn to a host cell comprising the vector of claim 4. The claims are broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claims encompass host cells that have been transfected with the vector of claims 5 or 6 that are comprised within a transgenic animal, including a human.

MPEP § 2105 [R-1] states:

> If the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter.

Amending claim 5 to recite "isolated" before "host cell" can obviate these grounds of rejection.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using an isolated mammary or prostate host cell comprising the vector of claim 4, does not reasonably provide enablement for any host cell comprising the vector of claim 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 5 and 6 are drawn to a host cell comprising the vector of claim 4. The claims are broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claims encompass host cells that have been transfected with the vector of claim 4 that are comprised within a transgenic animal, including nonhuman or human animals and animals treated using gene therapy.

Support for this interpretation of the claims can be found in the specification at, for example, page 43, lines 21-24, and page 83, line 28, to page 84, line 2.

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because the amount of guidance, direction, and exemplification set forth therein would not be sufficient to enable the skilled artisan to have a reasonable expectation of success in making and using the claimed invention without the need to perform additional, and an undue amount of experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification does not provide a sufficient amount of guidance, direction, or exemplification to enable the skilled artisan to make or use host cells that are comprised within a non-human transgenic animal. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predicable or viable. Houdebine (*Journal of Biotechnology* 1994, 34: 269-287) teaches the vectors to be used for directing the expression of transgenes in any given tissue, or in all tissues, must contain the appropriate regulatory regions. Houdebine teaches expression is heavily dependent on the site of integration in the host genome and the site of integration is presently unpredictable. Therefore, it is concluded that one of skill in the art would need to perform undue experimentation in order to make and use the claimed host comprised within a transgenic animal.

In addition, the specification does not teach provide a sufficient amount of guidance, direction, and exemplification to enable the skilled artisan to have a reasonable expectation of successfully producing host cells within a living organism, which comprise the vector of claims 4, by gene transfer, or *gene therapy*. The art of gene therapy, i.e., the *in vivo* delivery genetic information to targeted cells within a body using naked DNA or viral vectors or by reintroducing *ex vivo* modified host cells into the body, is still in its infancy. Moreover, the art is highly unpredictable and its successful application has been hindered by numerous limitations, which the specification does not remedy and would preclude the skilled artisan from having a reasonable expectation of successfully making and using the claimed invention without need of performing an undue amount of experimentation.

For example, the teachings of the specification have not overcome the problems with *in vivo* delivery and expression. Verma et al. (*Nature* 1997, **389**: 239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al. state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression. Similarly, Amalfitano et al. (*Current Gene Therapy* 2002, **2**: 111-133) teach that non-viral mediated transfer of DNA generally suffers from low transduction efficiencies. In addition, Amalfitano et al. discuss numerous limitations that have been encountered in using retroviral vectors to deliver DNA into a subject and teach the use

of adenoviral vectors can be ineffective because of the induction of strong immune responses in the host to the viral vectors and direct acute and chronic toxicity caused by the vector itself.

It is noted that Amalfitano et al. teach that a despite general lack of success, the first conclusive evidence that gene therapy can show efficacy in humans was achieved in human X-linked SCID subjects *via* retrovirus transduction. However, since the publication, The Department of Health and Human Services has released a memorandum dated January 14, 2003, a copy of which is attached to this Office action, that urges all such investigations to be discontinued until new data are available, the possible etiology and risks of adverse events associated are considered, and recommendations emerge. Despite the initial promise of the trial studying gene transfer as a possible treatment for the disease, investigators have found that retroviral-mediated insertion of the transgene has caused the subjects to develop cancer. The results of the trial underscore the high degree of unpredictability associated with the art and the fact that the skilled artisan could not make or use the claimed invention with a reasonable expectation of success without need to perform additional experimentation.

The state of the art, as a whole, is well defined by Pandha et al. (*Current Opinion in Investigational Drugs* 2000; **1** (1): 122-134) in the abstract. Pandha et al. teach:

> Despite the rapid technological advances that continue to sustain the field of cancer gene therapy, few individual patients have benefited from the revolution so far. The plethora of clinical trials described confirms that each malignancy will have its own ideal strategy based on the associated molecular defects, and there has been rapid progress from this viewpoint. At the same time, there has been a renewed appreciation for the limitations to gene therapy, which include low efficiency of gene transfer, poor specificity of response and methods to accurately evaluate responses, and lack of truly tumor-specific targets at which to aim. As with all new therapies, we are climbing a steep learning curve in terms of encountering treatment-related toxicities, as well as profound ethical and regulatory issues.

In view of the preponderance of evidence establishing the state of the art, now and at the time the application was filed, and the level of unpredictability associated therewith, in the absence of a disclosure of an amount of guidance, direction, and exemplification that is reasonably commensurate in scope with the claims, it appears that skilled artisan could not make and use the claimed invention with a reasonable

expectation of success without having the need to perform an undue amount of experimentation.

Amending claim 5 to recite "isolated" before "host cell" can obviate these grounds of rejection.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank EST Database Accession No. AA422178, 1997), as evidenced by a USPTO database search using SEQ ID NO: 5 as a query (see USPTO Search Report US-09-599-087-5.rst, result 2).

Applicant has traversed this ground of rejection arguing the prior art does not anticipate the claimed invention. Applicant' arguments are set forth at pages 23-26 of the Amendment filed November 20, 2003.

Applicant's arguments have been carefully considered, but not found persuasive for the following reasons:

Hillier et al. teach the polynucleotide sequence of an isolated nucleic acid molecule encoding an amino acid sequence that is 100% identical to the amino acid sequence set forth in SEQ ID NO: 5 over the region spanning from the amino acid at position 1 to the amino acid at position 76. According to the annotation of GENBANK Accession No. AA422178, the polynucleotide sequence of the complementary DNA (cDNA) molecule of Hillier et al. is contained in a modified vector originally designated pT7T3D. The recombinant vector comprising the polynucleotide sequence of the cDNA molecule was cloned in a host prokaryotic cell designated DH10B.

The nucleic acid molecule of Hillier et al. does not comprise the nucleotide sequence set forth in SEQ ID NO: 4; nor does the nucleic acid molecule of Hillier et al. comprise a nucleotide sequence encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 5. Nevertheless, **the nucleic acid molecule of Hillier et al. does comprise a polynucleotide sequence that is complementary to the nucleotide sequence of SEQ ID NO: 4, since the nucleic acid molecule of Hillier et al. comprises the polynucleotide sequence set forth between nucleotide residues 1 and 60, which is complementary to the polynucleotide sequence of SEQ ID NO: 4.** Therefore, Hillier et al. anticipates the invention of claim 1, which in this instance is interpreted as an isolated nucleic acid molecule *comprising* a nucleotide sequence complementary to the nucleotide sequence of SEQ ID NO: 4.

Additionally, although Hillier et al. does not teach that the nucleic acid molecule comprises the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755, the specification does not teach the actual polynucleotide sequence of the DNA insert. The specification discloses only that the DNA insert encodes a human SECS-1 polypeptide and has a polynucleotide sequence that differs from SEQ ID NO: 4 since, according to the disclosure at page 2, lines 26-29, the DNA insert comprises the polynucleotide sequence of an allelic variant or splice variant of the nucleotide sequence of SEQ ID NO: 4. The nucleic acid molecule of Hillier et al. has a polynucleotide sequence that differs from SEQ ID NO: 4, but which encodes an amino acid sequence that is 100% identical to the amino acid sequence set forth in SEQ ID NO: 5 over the region spanning from the amino acid at position 1 to the amino acid at position 76. Therefore, absent a showing of any difference, the nucleic acid molecule of Hillier et al. is deemed the same as the claimed nucleic acid molecule comprising the nucleotide sequence of the DNA insert in the ATCC Deposit No. PTA-1755, which necessarily encodes a variant of the polypeptide encoded by SEQ ID NO: 4. The Office, however, does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed product. In the absence of evidence to the contrary, the burden is upon the

applicant to prove that the claimed product is different than that taught by the prior art. At page 25 of the Amendment filed November 20, 2003, Applicant states the nucleic acid molecule of the prior art has a nucleotide sequence that differs from the nucleotide sequence of the DNA insert encoding a Secs-1 polypeptide of ATCC Deposit No. PTA-1755 and that the polypeptide encoded by the nucleic acid molecule of the prior art is not a variant of the polypeptide of SEQ ID NO: 5, but Applicant has provided no factual evidence to support these assertions. Accordingly, in the absence of any factual evidence to the contrary, the nucleic acid molecule is still deemed the same as the DNA insert encoding a Secs-1 polypeptide of ATCC Deposit No. PTA-1755.

With regard to claim 2, the nucleic acid molecule of Hillier et al. is deemed to *comprise* a region of the nucleotide sequence of both SEQ ID NO: 4 and, absent a showing of any difference, the DNA insert in ATCC Deposit No. PTA-1755, which encode a polypeptide of at least 25 amino acids, but not more than 80 amino acids, which upon injection into an animal would produce an antibody that binds to the polypeptide of SEQ ID NO: 5. Again, the Office does not have the facilities for examining and comparing Applicants' product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed product. Nevertheless, **the nucleic acid molecule of Hillier et al. comprises, for example, the region of the polynucleotide sequence of SEQ ID NO: 4 spanning nucleotide residues 29 to 130, which encodes amino acids 1-34 of SEQ ID NO: 5**. This region of the nucleic acid molecule of Hillier et al. is deemed anticipatory of the invention of claim 2, absent a showing of any difference, because the region appears to encode a polypeptide of at least 25 amino acids, but not more than 80 amino acids, which upon injection into an animal would produce an antibody that binds to the polypeptide of SEQ ID NO: 5. At page 25 of the Amendment, Applicant has stated although the nucleotide sequence of the nucleic acid molecule of the prior art comprises the region of the nucleotide sequence of SEQ ID NO: 4 spanning residues 29-130, Applicant disagrees with the Action's assertion that the nucleotide sequence of the nucleic acid molecule of the prior art comprises the region of the nucleotide sequence of SEQ ID NO: 4. Applicant argues

the prior art does not recite disclose fragments of the polypeptide encoded by the disclosed nucleic acid molecule, but the question is not whether or not the prior art discloses a fragment, but whether what is disclosed falls under the scope of the claims. Applicant has argued because no single member of the genus of nucleic acid molecules defined by claim 2 encodes a polypeptide of greater than 80 amino acids, the nucleotide sequence of the prior art, which encodes a polypeptide of 98 amino acids, does not anticipate the claim. However, claim 2 is drawn to a nucleic acid molecule **comprising** a region of the nucleotide sequence of both SEQ ID NO: 4 and, absent a showing of any difference, the DNA insert in ATCC Deposit No. PTA-1755, which encodes a polypeptide of at least 25 amino acids, but not more than 80 amino acids, which upon injection into an animal would produce an antibody that binds to the polypeptide of SEQ ID NO: 5. The region of the nucleotide sequence of SEQ ID NO: 4 or the DNA insert to which the claims refer, absent a showing of any difference, of which the nucleic acid molecule of the prior art is *comprised* is expected to encode a polypeptide of at least 25 amino acids, but not more than 80 amino acids, which upon injection into an animal would produce an antibody that binds to the polypeptide of SEQ ID NO: 5.

As for claim 3, claim 3 is only considered insofar as the claim is drawn to a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5, or comprising a nucleotide sequence that is complementary the nucleotide sequence encoding the polypeptide. Although the nucleic acid molecule of Hillier et al. does not comprise a nucleotide sequence encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 5, **the nucleic acid molecule of Hillier et al. does comprise a polynucleotide sequence that is complementary to the nucleotide sequence of SEQ ID NO: 4 encoding the polypeptide of SEQ ID NO: 5**. For example, the nucleic acid molecule of Hillier et al. comprises the polynucleotide sequence set forth between nucleotide residues 1 and 60, which is complementary to the polynucleotide sequence of SEQ ID NO: 4, or which is complementary to a nucleotide sequence encoding the polypeptide of SEQ ID NO: 5. Therefore, Hillier et al. anticipates the invention of claim 3.

15. Claims 1-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Database GENBANK Accession No. AA283751, as evidenced by the declaration under 37 CFR § 1.131 by Anthony J. Polverino and Roland Luethy filed September 25, 2002 as part of Paper No. 18, Hillier et al. (*Genome Research* **6**: 807-828, 1996), Exhibit A (a printout of Internet accessible information regarding GENBANK Accession No. AA283751), and Exhibit B (an email communication from Christa Prange of the IMAGE Consortium dated May 12, 2003 in reply to the Examiner's query made May 7, 2003).

Applicant has traversed this ground of rejection. Applicant's argument are set forth in the Amendment filed November 20, 2003 at pages 26-29.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

GENBANK Accession No. AA283751 teaches an isolated complementary DNA (cDNA) molecule, which, as evidenced by Exhibit A, was cloned into a modified vector originally designated pT7T3D and is contained in an isolated prokaryotic host cell designated DH10B. **This clone is available royalty-free through the IMAGE Consortium.** As evidenced by Exhibit B, an email communication from Christa Prange of the IMAGE Consortium, by **April or May of 1997**, the clone was made publicly available through the clone distributors. Hillier et al. describe the methods by which the isolation and procurement of the cDNA was accomplished.

Although the polynucleotide sequence of the isolated cDNA molecule of the prior art is reported as being different from the polynucleotide sequence set forth in SEQ ID NO: 4, the declaration by Anthony J. Polverino and Roland Luethy filed September 25, 2002 as part of Paper No. 18 provides evidence that the cDNA of the prior art is the same as the claimed nucleic acid molecule. The declaration states: (a) the amino acid sequence of an isolated polypeptide was determined by Applicants, (b) the determined amino acid sequence was used by Applicants as query in searching the databases to identify expressed sequence tags (ESTs) that are capable of encoding the isolated polypeptide, (c) GENBANK Accession No. AA283751 was identified by Applicants as containing sequences capable of encoding the polypeptide, (d) a clone containing the

nucleotide sequence purportedly disclosed as GENBANK Accession No. AA283751 was acquired by Applicants from the IMAGE Consortium, and (e) the polynucleotide sequence of the cDNA insert of the acquired clone was determined by Applicants. The declaration further states the polynucleotide sequence of the cDNA insert of the acquired clone is depicted in thereto attached Exhibit B; the declaration also states that the polynucleotide sequence depicted in Exhibit B is the same as the polynucleotide sequence set forth as SEQ ID NO: 4 in the application. Accordingly, the cDNA of the prior art is the same as the claimed nucleic acid molecule.

Applicant has appears to have argued the actual sequence of the cDNA molecule was not known prior to the filing date sought by Applicant. The evidence presented as Exhibit B shows the cDNA molecule was made publicly accessible as early as April or May of 1997. Although the polynucleotide sequence of the cDNA molecule of the prior art is, according to Applicants' declaration, different from the polynucleotide of the claimed nucleic acid molecule, **the polynucleotide sequence of a nucleic acid molecule is an inherent property**. The claims are drawn to a nucleic acid molecule having the same polynucleotide sequence as the nucleic acid molecule of the prior art, as evidenced by Applicants' declaration.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al. (GenBank EST Database Accession No. AA422178, 1997), as evidenced by a USPTO database search using SEQ ID NO: 5 as a query (see USPTO Search

Report US-09-599-087-5.rst, result 2), in view of Bendig (*Genet Eng* **7**: 91-127, 1988) and Niwa et al. (*Gene* **108**: 193-199, 1991).

Applicant has traversed this ground of rejection. Applicant's arguments are set forth at pages 29 and 30 of the Amendment filed November 20, 2003.

Applicant's arguments have been carefully considered but not found persuasive for the same reasons Applicant's arguments traversing the corresponding rejection under 35 USC § 102 were not.

18. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Database GENBANK Accession No. AA283751, as evidenced by the declaration under 37 CFR § 1.131 by Anthony J. Polverino and Roland Luethy filed September 25, 2002 as part of Paper No. 18, Hillier et al. (*Genome Research* **6**: 807-828, 1996), Exhibit A (a printout of Internet accessible information regarding GENBANK Accession No. AA283751), and Exhibit B (an email communication from Christa Prange of the IMAGE Consortium dated May 12, 2003 in reply to the Examiner's query made May 7, 2003) in view of Bendig (*Genet Eng* **7**: 91-127, 1988) and Niwa et al. (*Gene* **108**: 193-199, 1991).

Applicant has traversed this ground of rejection. Applicant's arguments are set forth at pages 29 and 30 of the Amendment filed November 20, 2003.

Applicant's arguments have been carefully considered but not found persuasive for the same reasons Applicant's arguments traversing the corresponding rejection under 35 USC § 102 were not.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
February 20, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600